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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Response to Arguments

Applicant's arguments filed 02/01/08 have been fully considered but they are not persuasive.

Applicant argues that because Shimizu's up to 50% MCC disclosure is not based on the total tablet weight but only on the weight of the additives portion, the Shimizu range of MCC is not overlapping or adjacent to the Applicants' claimed range of "at least 50%" of a silicified MCC. Thus, Shimizu does not teach or suggest the Applicants' claimed range of cellulose-based binder.

However, in response to applicant's arguments against Shimizu individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Shimizu is cited in combination with Sherwood for the claimed silicified MCC in the claimed amount. Further, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In the present case, the dosage form taught in Shimizu has the same disintegrating time as claimed by the present invention. Accordingly, the examiner is unable to determine any unexpected result over the specific amount of MCC being recited in the present claims.

Applicant argues that the Examiner relies on Sherwood's general teaching of the advantages of silicified MCC over MCC, along with Sherwood's working Examples 10-12 in which the exemplary tablets contain 70% silicified microcrystalline cellulose. But such a combination of teachings does not teach or suggest the Applicants' claimed range of binder. Assuming (without conceding) that MCC and silicified microcrystalline cellulose are interchangeable, the skilled worker would not have been motivated to increase the amount of silicified microcrystalline cellulose in Shimizu's hypothetically modified tablet to 70% based on Sherwood's working Examples 10-12. Increasing the amount of silicified microcrystalline cellulose in Shimizu's hypothetically modified tablet would have been expected to adversely affect the oral disintegratability of the tablet.

However, in response to applicant's argument that *"increasing the amount of silicified microcrystalline cellulose in Shimizu's hypothetically modified tablet would have been expected to adversely affect the oral disintegratability of the tablet"*, it is noted that while this statement might be true, it is not necessarily that increasing the amount of silicified MCC in Shimizu will decrease the disintegratability of the tablet. Evidence is cited in the present claims, "at least 50% silicified MCC...orally disintegratable within the range of 1 to 15 seconds" (see claims 1 and 7-8). While applicant repeatedly alleged that the amount of MCC taught by Sherwood would slow down the disintegrating time, applicant has not submitted evident to show the disintegrating time of Sherwood's dosage form. It is noted that Sherwood teaches the use of silicified MCC in the claimed amount to improve disintegration properties (column 2, line 46; and column 4, lines 50-51).

Sherwood discloses that "[b]oth microcrystalline cellulose and silicon dioxide are substantially water insoluble" (see Sherwood at col. 9, lines 21-22). Shimizu teaches the importance of having a water soluble additive such as a sugar alcohol (e.g. mannitol) in amounts of 5% to 97%, not including the weight of the fine granules (See col. 10 lines 1-13 of (Shimizu). Indeed, while the sugar may account for nearly all of the non-fine granule additives, the MCC may not. This is not too surprising given that Shimizu is making an orally disintegratable tablet. Sherwood further discloses that due to the use of silicified microcrystalline cellulose in place of MCC, "the amount of the novel excipient [silicified microcrystalline cellulose] compared to the amount of microcrystalline cellulose which must be used in a wet granulation technique to obtain an acceptable solid dosage form is substantially reduced" (emphasis added) (see Sherwood at col. 12, lines 9-13). Accordingly, there is no motivation to combine the teachings of Shimizu and Sherwood to obtain the Applicant's claimed orally disintegrating tablet containing at least 50 weight % of silicified microcrystalline cellulose.

However, in response to applicant's arguments, it is noted that the present claims also recite the use of silicon dioxide in order to obtain a rapidly disintegrating tablet (see claim 11). Moreover, as discussed above, Sherwood teaches a dosage form with improved disintegration properties. Accordingly, one of ordinary skill in the art would have been motivated to modify the rapid disintegrating tablet of Shimizu in view of the teachings of Sherwood to obtain the claimed invention, because Sherwood teaches

using silicified MCC in the claimed amount to improve not just the compressibility of the tablet, but also the disintegration properties (column 4, lines 50-67).

Applicant argues that one of ordinary skill in the art would not have been motivated to modify the teachings of Betzing based on Sherwood (or Shimizu) to replace Betzing's MCC with Sherwood's silicified microcrystalline cellulose to obtain the claimed tablet, nor would the skilled worker have had a reasonable expectation of success in doing so. As previously argued, a worker of ordinary skill in the art would expect from Betzing that the precise excipients in the specific ratios as disclosed throughout Betzing (e.g., col. 2, line 58 to col. 3, line 28) must be used, and that replacing Betzing's MCC with Sherwood's silicified microcrystalline cellulose would at best yield uncertain results and more likely would further slow the disintegration rate. Specifically, at column 3, lines 20-28, Betzing indicates that replacing MCC with either water soluble lactose or water insoluble calcium hydrogen phosphate results in a significant decrease in the disintegration rate (see also comparative Examples 6 and 7).

However, in response to applicant's argument that *Betzing indicates that replacing MCC with either water soluble lactose or water insoluble calcium hydrogen phosphate results in a significant decrease in the disintegration rate*, this statement in Betzing does not prevent and/or preclude one of ordinary skill in the art to replace MCC with the MCC taught by Shimizu and Sherwood, since Sherwood teaches the use of silicified MCC to improve compressibility and disintegratability properties.

Applicant argues that the Examiner fails to address the deficiency in Sherwood, namely that Sherwood fails to teach or suggest the suitability of using silicified MCC in forming an orally disintegrating tablet. Note that "disintegration" is not tantamount to oral disintegration as used in Shimizu or the present application. Most immediate release tablets contain a "disintegrant," yet most tablets do not dissolve in the patient's mouth in less than 15 seconds.

In response to applicant's argument that most immediate release tablets contain a "disintegrant," yet most tablets do not dissolve in the patient's mouth in less than 15 seconds, however, Sherwood teaches tablet containing silicified MCC in the claimed amount to improve disintegratability properties, the burden is shifted to applicant to show that the tablet taught by Sherwood does not disintegrate rapidly. However, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Sherwood is cited in combination with Shimizu for the teaching of rapidly disintegrate tablet having disintegrating time less than 30 seconds.

Applicant argues that because replacing Betzing's MCC with Sherwood's silicified microcrystalline cellulose would have unpredictable results, and likely an undesirable decrease in disintegration rate, one of ordinary skill in the art would not have found the present invention, which requires faster oral disintegration rates, to have been obvious.

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Accordingly, claims 1, 5, 7-9 and 11-37 would not have been obvious over Betzing in combination with Shimizu and Sherwood.

However, it is noted that applicant's statement that the disintegration rate is likely to be decreased by replacing the MCC is not supported with any factual data. Shimizu teaches using MCC having the claimed particle size results in a rapid disintegration rate. Sherwood teaches the use of silicified MCC is known in the art to improve disintegration properties. As discussed above, Sherwood does not explicitly teach the dissolution rate, does not necessarily mean that the dissolution rate of Sherwood is slow. Applicant's attention is called to the teaching in Sherwood at column 4, lines 50-67, Sherwood teaches the dissolution rate is improved.

/S. Tran/
Primary Examiner
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